

EXHIBIT 7

RESULTS

In normal individuals, a very low basic expression of ICOS can be observed on up to 10 - 14% of T cells in the peripheral blood using a very sensitive (phycoerythrin-based) detection system (Beier *et al.*, 2000, "Induction, binding specificity and function of human ICOS," Eur. J. Immunol. 30:3707-17, attached hereto as Exhibit A). In the four allergic individuals studied, ICOS was present on 8.3 % to 31.5% of peripheral blood T cells (FIGS. 1 and 2). This result may suggest that some allergic individuals express higher basic levels of ICOS on T cells in the peripheral blood.

In the bronchoalveolar fluid 39.4% to 69.3% of all T cells carried the ICOS antigen on the surface. In the "negative" T cell population the median of the signal was higher when compared to the peripheral blood, indicating that even most of the "negative" T cells carried low levels of ICOS (FIG. 1). In all four patients studied, the percentage of ICOS-expressing T cells in the BAL was substantially higher when compared to peripheral blood T cells of the same individuals analyzed in parallel (FIG. 2).

Bronchial biopsies taken 42 hours after segmental allergen provocation from the 4 lavaged patients were analyzed by immunohistology. In addition, bronchial biopsies taken from another 4 allergic asthmatics were examined. Characteristically, numerous ICOS positive T cells were found in the bronchial epithelium and the submucosa (FIG. 3). The proportion of ICOS positive cells found at these anatomical sites was compatible with the percentages of ICOS positive T cells found in the BAL using flow cytometry.

In the non-inflamed lung barely any T cells can be found. In the lung tissue of allergic asthmatics a substantial T cell infiltration is typically observed.

Attachments

FIG.1

Flow cytometry profiles obtained with cells from patient 4. In the peripheral blood, 55.4% of all cells bore the CD3 marker (and were thus identified as T cells) and 8.3% of them expressed ICOS. In the bronchoalveolar lavage the gated population contained 46.6% CD3-positive cells and 40.6% of them expressed

ICOS. Note that the numbers given in the right upper quadrants represent percentages of ICOS-positive T cells analyzed.

FIG. 2

Percentage of ICOS-positive T cells in the peripheral blood and bronchoalveolar lavage fluid of four patients with allergic asthma 42 hours after segmental allergen provocation.

FIG. 3

Immunohistological staining of ICOS positive T cells (stained in red) in a representative human bronchial biopsy. Ep=Epithelium; BM= basal membrane; SM=submucosa.

Exhibit A.

Beier *et al.*, 2000, "Induction, binding specificity and function of human ICOS," Eur. J. Immunol. 30:3707-17.

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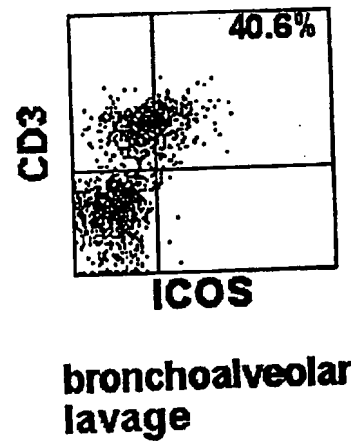
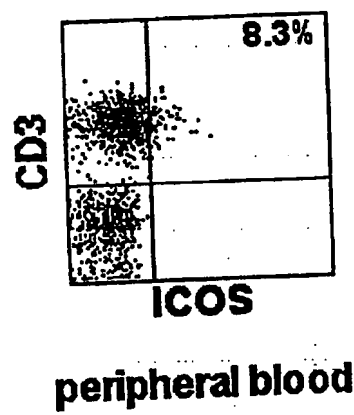


FIG. 1

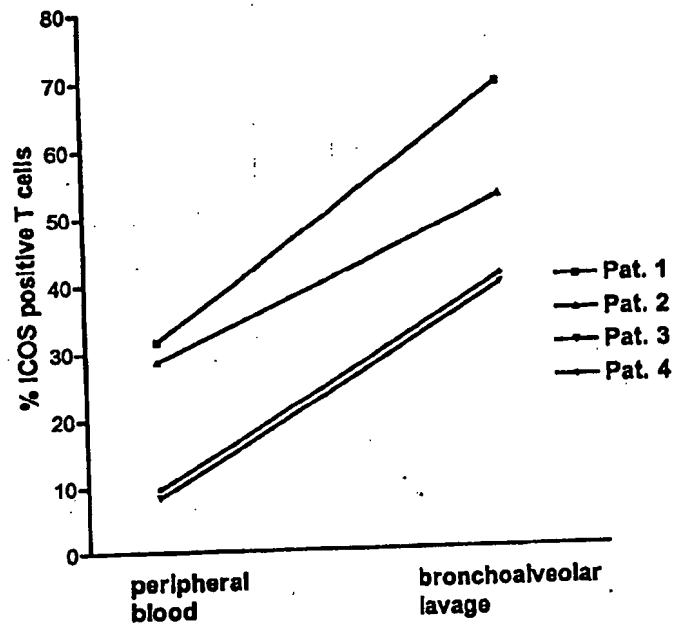


FIG. 2

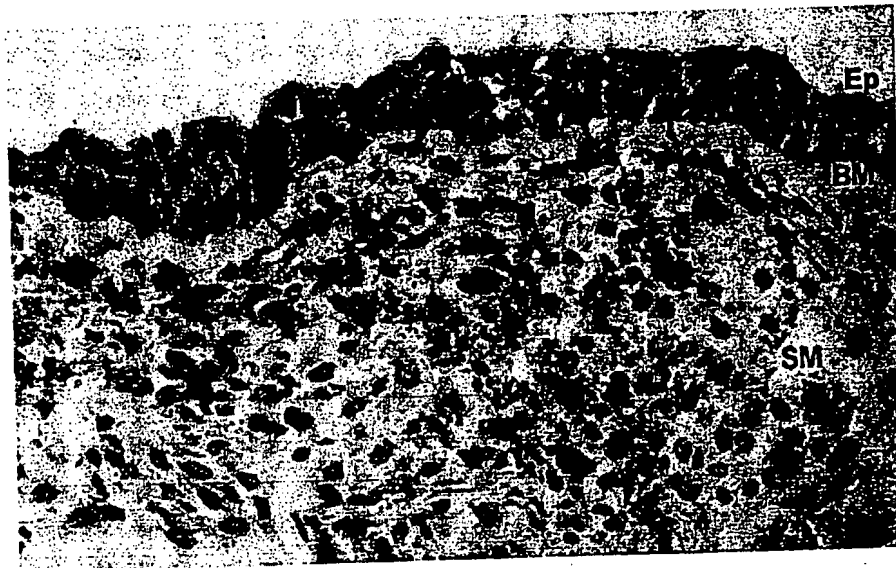


FIG. 3